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Claims

1. Method for the identification and quantification of one or more proteins in a sample containing a mixture of proteins, wherein said method comprises the steps of:
   a) Providing a sample which contains a mixture of proteins;
   b) Providing a reagent for the analysis of peptides which has the general formula

   A-Y-PRG

   in which
   A constitutes at least one functional group for the reversible, covalent or non-covalent binding to a support material,
   Y is a group comprising at least one chelate function for metals being low in isotopes, and
   PRG is a reactive group for the selective binding to peptides or other biomolecules to be analyzed;
   c) Cleaving the proteins in the sample in order to produce peptides;
   d) Coupling the peptides to the reagent of step b);
   e) Selecting the peptides labeled in step d) under the employment of a functional group for the reversible, covalent or non-covalent binding to a support material and removal of the unbound peptides;
   f) Releasing the bound peptides from the support material and elution from the matrix; and
   g) Detecting and identifying the labeled peptides by means of mass spectrometry.

2. Method according to claim 1, wherein the cleavage of the peptides is performed enzymatically or chemically.

3. Method according to claim 1 or 2, wherein the labeled peptides, after their release from the support material and before their analysis by mass spectrometry, are separated from each other, in particular by means of HPLC.

4. Method according to one of the claims 1 to 3, characterized in that several protein- and/or peptide-containing samples are analyzed together.

5. Method according to one of the claims 1 to 4, moreover comprising the sequencing of the labeled peptides.

6. Method for the detection of the relative expression of proteins in a protein-containing sample, wherein said method comprises the steps of:
   a) Providing a biological sample which contains proteins;
   b) Providing a reagent for the analysis of peptides which has the general formula

A-Y-PRG

in which

A constitutes at least one functional group for the reversible, covalent or non-covalent binding to a support material,

Y is a group comprising at least one chelate function for metals being low in isotopes, and

PRG is a reactive group for the selective binding to peptides or other biomolecules to be analyzed;

   c) Cleaving the proteins in the sample in order to produce peptides;
   d) Coupling the peptides to the reagent of step b);
   e) Selecting the peptides labeled in step d) under the employment of a functional group for the reversible, covalent or non-covalent binding to a support material and removal of the unbound peptides;
   f) Releasing the bound peptides from the support material and elution from the matrix; and
   g) Detecting and identifying the labeled peptides by means of mass spectrometry;
   h) Measuring the relative occurrence of the differently labeled peptides as distinct peaks of ions in order to determine the relative expression of the protein, from which the affinity-labeled peptide is derived.

7. Method according to one of the claims 1 to 6, characterized in that the arrangement of the groups A, X and PRG is interchanged.

8. Method according to one of the claims 1 to 7, characterized in that the labeled peptides are detected by means of tandem techniques, like e.g. matrix-assisted laser desorption/ionization (MALDI) time-of-flight (TOF)-TOF-MS and electrospray ionization (ESI)-MS.

9. Reagent for the mass spectroscopic analysis of peptides which has the general formula

A-Y-PRG

in which
A constitutes at least one functional group for the reversible, covalent or non-covalent binding to a support material,
Y is a group comprising at least one chelate function for metals being low in isotopes, and
PRG is a reactive group for the selective binding of peptides or other biomolecules to be analyzed, that shall be analyzed.

10. Reagent according to claim 9, wherein the arrangement of the groups A, Y and PRG is interchanged.

11. Reagent according to claim 10 or 11, wherein the PRG is selected from the group consisting of a sulfhydryl-reactive group, an amine-reactive group and an enzyme substrate.

12. Reagent according to claim 11, wherein the PRG is selected from the group consisting of an amine-reactive pentafluorophenyl ester group, an amine-reactive N-hydroxysuccinimide ester group, sulfonylhalide, isocyanate, isothiocyanate, active ester, tetrafluorophenyl ester, an acid halide and an acid anhydride, a homoserine lactone-reactive primary amine group and a carboxylic acid-reactive amine, alcohol or 2,3,5,6-tetrafluorophenyltrifluoro-acetate, a iodine acetylamide group, an epoxide, an α-haloacyl group, a nitrile, a sulfonated alkyl, an arylthiol and a maleimide.

13. Reagent according to one of the claims 9 to 12, wherein A is selected from the group consisting of biotin or modified biotin, a 1,2-diol, glutathione, maltose, a nitrilotriacetic acid group, an oligohistidine and a hapten or other reactive reagents allowing for a reversible binding to a support material.

14. Reagent according to one of the claims 9 to 13, moreover comprising a linker between the groups A, Y and/or PRG, which is cleavable in a chemical and/or enzymatic way and/or by exposure to radiation or light.

15. Reagent according to claim 14, wherein the linker contains a disulfide group.

16. Reagent according to one of the claims 9 to 15, wherein Y is selected from the group consisting of a macrocyclic lanthanoid chelate complex, a functionalized tetraaza-macrocycle, a polyaza-polyacetic acid, DOTA, a DOTA-derivative, NOTA, a NOTA-derivative, 1,4,7,10,13,16,19,22-octaazacyclotetracosane-1,4,7,10,13,16,19,22-octaacetic acid (OTEC), 1,4,7,10,14-17,20,23-octaazacyclohexacosane-1,4,7,10,14,17,20,23-octaacetic acid (OHEC), EDTA, DTPA-BP, DTPA, DO3A, HP-DO3A and DTPA-BMA.

17. Reagent according to one of the claims 9 to 16, wherein the metal bound by the chelate complex is selected from Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tm, V, W, Y, Yb and Zn.

18. Reagent according to one of the claims 9 to 17, wherein the chelate forming group is labeled with several different metals.

19. Use of a reagent according to one of the claims 9 to 17 for the detection of peptides in a biological sample and/or for determining the relative expression of proteins in a protein-containing sample.

20. Use of a reagent according to one of the claims 9 to 17 for the diagnosis of diseases of an animal, in particular of the human, by detecting the relative expression of proteins in a protein-containing sample taken from the animal.

21. Diagnostic kit, containing a reagent according to one of the claims 9 to 17 together with further substances and/or enzymes suitable for the detection of peptides in a biological sample and/or the determination of the relative expression of proteins in a protein-containing sample, in particular containing an internal standard.